UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: APR 21 1981

SUBJECT: Status Report* 8EHQ-1180-0373S
8EHQ-1180-0374S
8EHQ-0281-0373S Supplement
8EHQ-0281-0374S Supplement

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Revision Needed

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Submission Description

The 3M Company has submitted preliminary reports with test protocols and the final reports of a teratology study in rats with 1) a mixture of N-ethyl perfluorooctylsulfonamido ethanol and N-ethyl perfluoroheptylsulfonamido ethanol (8EHQ-1180-0373S; 8EHQ-0281-0373S Supplement) and 2) FC-95, a commercial mixture of perfluoroalkylsulfonic acid potassium salts (8EHQ-1180-0374S and 8EHQ-0281-0374S Supplement). In addition, submission 8EHQ-1180-0374S contains a 3M technical report entitled "Analysis of Selected Decatur Employee Serum for Sulfonic and Carboxylic Fluorochemicals".

According to the submitted protocols, the tested mixtures were administered via oral intubation to sexually mature, time-mated female rats on days 6 through 15 of gestation. Animals were assigned to groups receiving 0, 1, 5 or 10 mg/kg/day of the potassium salt derivative mixture or 0, 25, 37.5 or 75 mg/kg/day of the perfluoroethanol derivative mixture.

The final teratology reports (8EHQ-0281-0373S Supplement and 8EHQ-0281-0374S Supplement) state that both test mixtures produced a "developmental eye abnormality which appeared to be an arrest in development of the primary lens fibers forming the embryonal lens nucleus, followed by secondary aberrations of the secondary lens fibers of the fetal nucleus". According to the final reports, this effect was observed in all three dose groups administered FC-95 (significant in the high dose group) and was significantly higher than controls in all three dose groups administered the mixture of perfluoroethanol derivatives. The final reports further state that, while FC-95 did not produce an increase in skeletal abnormalities, the mixture of

*NOTE: This status report is the result of a preliminary staff evaluation of information submitted to EPA. Statements made herein are not to be regarded as expressing final Agency policy or intent with respect to this particular chemical. Any review of the status report should take into consideration the fact that it may be based on incomplete information.

perfluoroethanol derivatives produced cleft palates in the high and mid dose groups (significant in the high dose group), blood in the fetal kidney parenchyma in all three dose groups (significant in the high dose group), and malformations in fetal sternebrae and other skeleton aberrations of varying significance at the different dose levels. The final reports also state that FC-95 at the high dose and the perfluoroethanol derivative mixture at the high and mid doses were maternally toxic in reducing weight gain during dosing, but did not affect the ovaries or reproductive tract contents of the dams and were not embryotoxic.

In the submitted 3M technical report, it is stated that fluorochemicals have been detected in the blood of 3M employees. According to that 3M report, the five highest fluorine-containing serum samples among ten selected plant employees contained three fluorochemicals with total levels ranging from 4.1 to 11.8 ppm.

The submitter also states that according to employee records and a recent study conducted by the 3M Company which was published in the American Industrial Hygiene Association Journal (Vol. 41:584-589, August, 1980) "to date no human health problems have been observed nor disease patterns detected which are attributable or related to fluorochemical exposure". This published study, entitled "Health Status of Plant Workers Exposed to Fluorochemicals - A Preliminary Report," contains information on fluorochemical levels both in the blood of fluorochemical plant workers and in workplace ambient air, as well as the results of employee health screening examinations and a retrospective epidemiological investigation of plant employees. The published study indicates that analysis of fluorine levels in the blood of ammonium perfluorooctanoate production workers showed that although inorganic fluorine levels were comparable to normal human sera, organic fluorine levels ranged from 1.00 to 71.00 ppm, compared to 0.01 to 0.13 ppm for normal human sera. The published report also states that one worker with elevated organic fluorine in the blood was moved to a fluorochemical-free plant location and monitored for blood and urine fluorine at regular intervals. Over an 18 month period, the serum organic fluorine levels in this worker reportedly decreased from 70 to 39 ppm, and levels of perfluorooctanoate in the urine (24 hour collections) decreased from 387 to 80 micrograms over the first 14 months of this period. The report states that these blood and urine values "suggest that some fluorochemicals are very slowly eliminated in humans".

According to the same published 3M study, the results of 3M employee medical examinations, which included liver function profiles, showed no relationship between test result deviations and blood levels of organic fluorine. The most frequently encountered liver enzyme exceeding the normal range among a

sample of all plant employees was serum gamma-glutamyl-transferase (SGGT). However the 3M study states that these deviations "were most likely unrelated to plant work and are compatible with the individuals' predisposition toward alcohol".

The 3M published study also states that a retrospective cohort mortality study of plant employees covering a 30 year period from 1948 to 1978 indicated no disagreement between observed and expected mortality among employees in general or chemical workers in particular. The report states further that this finding was true for all causes of death and specific causes of death due to cancer.

In the same publication, it is reported that ammonium perfluoro-octanoate was negative in the Ames test both with and without metabolic activation. The target organ of this same substance in rodents was reported to be the liver, where a more pronounced histopathological effect was observed in males than in females. The published report also states that the major site of toxicity in the rhesus monkey appeared to be the reticuloendothelial system. The published report states that details of these studies are presented in a separate publication. However, this separate publication was not cited.

According to the 3M published report, air monitoring in the operator's breathing zone indicated fluorochemical levels up to 3.27 mg/m^3 during fluorochemical processing and packaging operations, but that this level has been reduced to 0.47 mg/m^3 by instituting appropriate modifications which were described in the report.

Submission Evaluation

The final reports provided in submissions 8EHQ-0281-0373S Supplement and 8EHQ-0281-0374S Supplement furnish detailed teratology data for the subject mixtures, both of which contain organofluorine compounds and produce malformations during fetal development, particularly failure of the eye lens to develop normally. Such failure occurs rarely. These submissions report for the first time that this type of teratogenic effect can be induced by exogenous chemicals. Additional research with these fluorochemical mixtures appears to be needed to determine the mechanism of lens teratogenesis.

The 3M sponsored epidemiology study reported in the American Industrial Hygiene Association Journal appears to be too general for detecting slowly developing clinical toxicity resulting from exposure to special classes of organic compounds. The interesting data in this published report are that 1) workers exposed to the perfluoro compounds can absorb them, as indicated by blood

and urine levels, and 2) the one worker studied for several months after exposure had been terminated still had organic fluorine in the blood at 18 months and was still excreting perfluorooctanoate in the urine at 14 months. (It should be noted that fecal elimination was not monitored). The blood level of organic fluorine had decreased to approximately one half, and the urine level of perfluorooctanoate by approximately 80%. This finding indicates a blood half-life of at least one and one-half years. The provided data do not permit a determination of whether there is firm bonding with plasma proteins or whether there is continuous release from depot stores in the body. Firm bonding is suggested by the increasing ratio of serum levels of organic fluorine to urinary levels of perfluorooctanoate, as though less and less of the amount in the blood can be excreted by the kidneys. This ratio of organic serum in the blood to perfluorooctanoate in the urine increased from 17 at one week post-exposure to 55 at 14 months post-exposure. The data also suggest that the perfluoroates are picked up by macrophages, stored in the reticuloendothelial system (liver, spleen, lungs, lymphatic structures and possibly the kidneys) and slowly released into the blood. These suggestions can be answered only by experiments on animals. The reported determinations on the studied employee did not include blood and urine levels of inorganic (ionized) fluorine.

It should be pointed out that although fluorine compounds affect bone, teeth and enzymes involved in blood clotting and thyroid gland functions, the published 3M report did not contain data pertaining to these parameters. The consulting hepatologist cited in this same published report may have been correct in assuming that the slightly elevated SGGT reflected "dispositions of the subjects to alcohol". However, no corroborating data were presented, nor was the possibility of storage in the liver considered. It appears that comprehensive animal studies on the pharmacokinetics and tissue levels of the subject chemicals in the reticulo-endothelial system are needed. Also, levels of organic and inorganic fluoride in the blood and urine, dental examinations and x-ray examination of bones for signs of fluorosis for each exposed person would allow a more complete evaluation of worker health status.

Current Production and Use

A review of the production range (includes importation volumes) statistics for N-ethyl perfluorooctylsulfonamido ethanol (CAS No. 1691-99-2), which is listed in the initial TSCA Inventory, has shown that between 100,000 and 1,000,000 pounds of this chemical were produced/imported in 1977. **/

A review of the production range (includes importation volumes) statistics for N-ethyl perfluoroheptylsulfonamido ethanol (CAS No. 68555-73-7), which is listed in the initial TSCA Inventory has shown that between 10,000 and 100,000 pounds of this chemical were produced/imported in 1977 **/

The submitter states that the mixture of the above two chemicals is used as an intermediate in the production of various finished fluorochemical products. The actual identity of this intermediate has been claimed by the submitter as "Confidential Business Information".

FC-95 is identified by the submitter as FLUORAD® Brand Fluorochemical Surfactant, a mixture containing potassium salts of homologous perfluoroalkyl sulfonates. The components of this mixture and their combined production volume have been claimed by the submitter as "Confidential Business Information".

The submitter states, in 8EHQ-1180-0374S, that this homologous mixture (or the corresponding ammonium salts) is currently sold as various products containing from 100 percent "solids" to 0.58 percent of the mixture. These products and their customer uses are described in the submission as follows:

FLUORAD® Brand Fluorochemical Surfactant, FC-95	Chrome Plating
FLUORAD® Brand Etching Bath Additive FC-93 (corresponding ammonium salt of the subject chemical)	Electronic Manufacturing
FLUORAD® Brand Fluorochemical Surfactant, FC-99 (corresponding amine salt of subject chemical)	Chrome Plating

**/ This production range information does not include any production/importation data claimed as confidential by the person(s) reporting for the TSCA Inventory, nor does it include any information which would compromise Confidential Business Information. The data submitted for the TSCA Inventory, including production range information, are subject to the limitations contained in the Inventory Reporting Regulations (40 CFR 710).

LIGHT WATER® Brand Aqueous Film Forming Foam FC-203	Fire Suppression
LIGHT WATER® Brand Aqueous Film Forming Foam FC-203A	Fire Suppression
LIGHT WATER® Brand Aqueous Film Forming Foam, FC-206A	Fire Suppression
LIGHT WATER® Brand Aqueous Film Forming Foam Alcohol Type Concentrate, FC-600	Fire Suppression
AFFF 6% Concentrate, FC-780B	Fire Suppression

No other information on current production volumes or uses of FC-95 were located in the secondary sources consulted.

Comments/Recommendations

The 3M Company states that it plans to inform all customers and employees with significant exposure potential to the subject chemicals of the teratology study findings and to outline 3M's recommendations for handling and using these products. The submitter also states that copies of these submissions are being transmitted to NIOSH and that the following work is planned for initiation in the near future: 1) a second teratology study designed to further evaluate these findings in both rats and rabbits; 2) lifetime feeding studies in rats; 3) development of industrial hygiene procedures designed to further reduce exposure to plant employees.

The EPA has evaluated a previous 3M submission (8EHQ-1077-0011) in which it was reported that FC-70, a commercial product used as an electronics vapor soldering fluid, decomposes to highly toxic perfluoroisobutylene and an unidentified perfluoroimine when overheated.

a) The 3M Company will be asked if it plans to conduct further monitoring studies (e.g., organic and inorganic fluoride levels in the blood and urine, dental examination and x-ray examinations of bones for signs of fluorosis) of employees potentially exposed to the subject chemicals.

b) The 3M Company will be requested to provide bibliographic citations for the mutagenicity and target organ studies in rodents and monkeys cited and summarized in the 3M report published in the American Industrial Hygiene Association Journal which is referenced in the original submissions.

c) It is recommended that the chemicals referenced in this status report be considered for inclusion in TSCA Section 8(a) Level A reporting.

d) The Chemical Hazard Identification Branch will consider the preparation of Chemical Hazard Information Profiles on selected chemicals within the class of perfluoroalkylsulfonates.

e) The Chemical Hazard Identification Branch will transmit a copy of this status report to OSHA, NIOSH, CPSC and OWWM/EPA. CHIB will also provide a copy of the status report to the Office of Toxics Integration (OTI/EPA) for appropriate distribution. The Industry Assistance Office (IAO/EPA) should consider sending the same information to the manufacturers and/or importers of the subject chemicals as listed in the Master TSCA Inventory, and to identified industry-associated organizations.